Notice of References Cited

Application/Control No.	Applicant(s)/Patent Under Reexamination	
11/593,758	SUZUKI ET AL.	
Examiner	Art Unit	Page 1 of 1
Joseph S. Kudla	1611	

U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-2005/0153977	07-2005	Sugasawa et al.	514/254.02
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Mutschler et al., Drug Actions: Basic Principles and Therapeutic Aspects, 1995, CRC Press, Pages 6-8.
	V	
	W	
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

Appendix A1

phenyl or thienyl, each of which is substituted with 1 to 3 halogen atoms (when substituted with 2 or 3 halogen atoms, the halogen atoms may be identical or different.).

R^2 in the compound of the general Formula (I) is preferably a group represented by the general Formula (II); more preferably, a group represented by the general Formula (II) wherein n is 2, m is 2, and X is a group represented by $N\text{-}R^{26}$ or $C(\text{-}R^{27})\text{-}R^{28}$; still more preferably, 4-(piperidin-1-yl)piperidin-1-yl, 4-propylpiperidin-1-yl, 4-cyclohexylpiperazin-1-yl, or 4-propylpiperazin-1-yl.

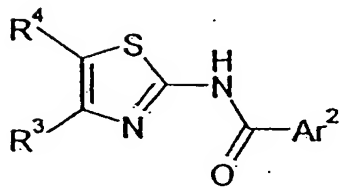
(2) The pharmaceutical composition according to (1) wherein R^1 is phenyl or thienyl, each of which may be substituted with 1 to 3 halogen atoms (when substituted with 2 or 3 halogen atoms, the halogen atoms may be identical or different); R^2 is a group represented by the general Formula (II), (wherein n is 2, m is 2, and X is a group represented by $N\text{-}R^{26}$ or $C(\text{-}R^{27})\text{-}R^{28}$); and Ar^1 is phenyl or pyridyl, each of which may be substituted.

(3) The pharmaceutical composition according to (1) or (2), wherein the pharmaceutical composition is used as a therapeutic agent for thrombocytopenia.

(4) The pharmaceutical composition according to (1) or (2), wherein the pharmaceutical composition is used as a c-Mpl ligand.

(5) A 2-acylaminothiazole derivative represented by the following general Formula (V) or a pharmaceutically acceptable salt thereof:

Appendix A1
cont'd



(V)

wherein symbols have the following meaning,

Ar^2: a group represented by Ar^1 as described in (1), with the proviso that indol-2-yl is excluded,

R^3: a group represented by R^1 as described in (1),

R^4: a group represented by R^2 as described in (1), with the proviso that a group represented by the general Formula (IV) is excluded.

Ar^2 in the compound of the general Formula (V) is preferably phenyl or monocyclic aromatic heterocycle, each of which may be substituted;

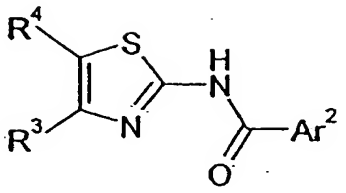
more preferably, phenyl or pyridyl, each of which may be substituted;

still more preferably, phenyl which is unsubstituted at 2- and 6-positions, substituted with -H, -F, -Cl, or -Br at 3-position, substituted with -F, -Cl, or -Br at 5-position, and substituted at 4-position, or pyridin-3-yl which is unsubstituted at 2- and 4-positions, substituted with -F, -Cl, or -Br at 5-position, and substituted at 6- position;

most preferably, phenyl substituted at 4-position with a substituent group selected from the group consisting of $-O-R^Y$, $-NH-R^Y$, optionally substituted piperidin-1-yl and optionally substituted piperazin-1-yl, or pyridin-3-yl which is substituted at 6-position with a substituent group selected from the group consisting of $-O-R^Y$, $-NH-R^Y$, optionally substituted piperidin-1-yl and optionally substituted piperazin-1-yl.

R^3 in the compound of the general Formula (V) is preferably phenyl or

Appendix A2



(V)

wherein symbols have the following meaning,

Ar^2: a group represented by Ar^1 as described in (1), with the proviso that indol-2-yl is excluded,

R^3: a group represented by R^1 as described in (1),

R^4: a group represented by R^2 as described in (1), with the proviso that a group represented by the general Formula (IV) is excluded.

Ar^2 in the compound of the general Formula (V) is preferably phenyl or monocyclic aromatic heterocycle, each of which may be substituted;

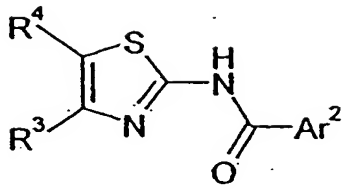
more preferably, phenyl or pyridyl, each of which may be substituted;

still more preferably, phenyl which is unsubstituted at 2- and 6-positions, substituted with -H, -F, -Cl, or -Br at 3-position, substituted with -F, -Cl, or -Br at 5-position, and substituted at 4-position, or pyridin-3-yl which is unsubstituted at 2- and 4-positions, substituted with -F, -Cl, or -Br at 5-position, and substituted at 6- position;

most preferably, phenyl substituted at 4-position with a substituent group selected from the group consisting of -O-R^Y, -NH-R^Y, optionally substituted piperidin-1-yl and optionally substituted piperazin-1-yl, or pyridin-3-yl which is substituted at 6-position with a substituent group selected from the group consisting of -O-R^Y, -NH-R^Y, optionally substituted piperidin-1-yl and optionally substituted piperazin-1-yl.

R^3 in the compound of the general Formula (V) is preferably phenyl or

Appendix A_3



(V)

wherein symbols have the following meaning,

Ar^2: a group represented by Ar^1 as described in (1), with the proviso that indol-2-yl is excluded,

R^3: a group represented by R^1 as described in (1),

R^4: a group represented by R^2 as described in (1), with the proviso that a group represented by the general Formula (IV) is excluded.

Ar^2 in the compound of the general Formula (V) is preferably phenyl or monocyclic aromatic heterocycle, each of which may be substituted;

more preferably, phenyl or pyridyl, each of which may be substituted;

still more preferably, phenyl which is unsubstituted at 2- and 6-positions, substituted with -H, -F, -Cl, or -Br at 3-position, substituted with -F, -Cl, or -Br at 5-position, and substituted at 4-position, or pyridin-3-yl which is unsubstituted at 2- and 4-positions, substituted with -F, -Cl, or -Br at 5-position, and substituted at 6- position;

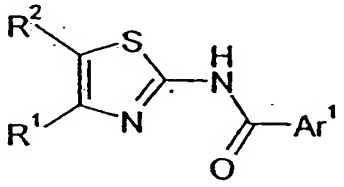
most preferably, phenyl substituted at 4-position with a substituent group selected from the group consisting of -O-R^Y, -NH-R^Y, optionally substituted piperidin-1-yl and optionally substituted piperazin-1-yl, or pyridin-3-yl which is substituted at 6-position with a substituent group selected from the group consisting of -O-R^Y, -NH-R^Y, optionally substituted piperidin-1-yl and optionally substituted piperazin-1-yl.

R^3 in the compound of the general Formula (V) is preferably phenyl or

Appendix A3
cont'd

The present invention relates to the following aspects (1)~(17).

(1) A pharmaceutical composition for increasing the number of platelets comprising a 2-acylaminothiazole derivative represented by the following general Formula (I) or a pharmaceutically acceptable salt thereof as an active ingredient:



(I)

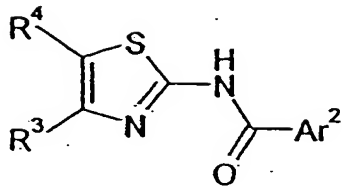
wherein symbols have the following meanings:

Ar^1: aryl, monocyclic aromatic heterocycle, or bicyclic condensed heterocycle, each of which may be substituted (with the proviso that when R^1 is aryl or pyridyl, each of which may be substituted with one or more groups selected from the group consisting of lower alkyl, -CO-lower alkyl, -COO-lower alkyl, -OH, -O-lower alkyl, -OCO-lower alkyl, and halogen atom, and R^2 is a group represented by the following general Formula (II); Ar^1 is not phenyl or pyridyl, each of which may be substituted with one or more groups selected from the group consisting of lower alkyl, -CO-lower alkyl, -COO-lower alkyl, -OH, -O-lower alkyl, -OCO-lower alkyl, and halogen atom.),

R^1: aryl or monocyclic aromatic heterocycle, each of which may be substituted,

R^2: a group represented by the following general Formula (II), (III) or (IV):

Appendix A4



(V)

wherein symbols have the following meaning,

Ar^2: a group represented by Ar^1 as described in (1), with the proviso that indol-2-yl is excluded,

R^3: a group represented by R^1 as described in (1),

R^4: a group represented by R^2 as described in (1), with the proviso that a group represented by the general Formula (IV) is excluded.

Ar^2 in the compound of the general Formula (V) is preferably phenyl or monocyclic aromatic heterocycle, each of which may be substituted;

more preferably, phenyl or pyridyl, each of which may be substituted;

still more preferably, phenyl which is unsubstituted at 2- and 6-positions, substituted with -H, -F, -Cl, or -Br at 3-position, substituted with -F, -Cl, or -Br at 5-position, and substituted at 4-position, or pyridin-3-yl which is unsubstituted at 2- and 4-positions, substituted with -F, -Cl, or -Br at 5-position, and substituted at 6- position;

most preferably, phenyl substituted at 4-position with a substituent group selected from the group consisting of -O-R^Y, -NH-R^Y, optionally substituted piperidin-1-yl and optionally substituted piperazin-1-yl, or pyridin-3-yl which is substituted at 6-position with a substituent group selected from the group consisting of -O-R^Y, -NH-R^Y, optionally substituted piperidin-1-yl and optionally substituted piperazin-1-yl.

→ R^3 in the compound of the general Formula (V) is preferably phenyl or

Appendix A4
cont'd

thienyl, each of which may be substituted; more preferably, phenyl or thienyl, each of which may be substituted with one or more groups selected from the group consisting of halogen atom and trifluoromethyl; still more preferably, phenyl or thienyl, each of which is substituted with 1 to 3 halogen atoms (when substituted with 2 or 3 halogen atoms, the halogen atom may be identical or different.)

R^4 in the compound of the general Formula (V) is preferably a group represented by the general Formula (II), more preferably a group represented by the general Formula (II) wherein n is 2, m is 2, and X is N-R^{26} or C-(R^{27})-R^{28}; still more preferably, 4-(piperidin-1-yl)piperidin-1-yl, 4-propylpiperidin-1-yl, 4-cyclohexylpiperazin-1-yl, or 4-propylpiperazin-1-yl.

(6) The compound according to (5), wherein Ar^2 is phenyl or monocyclic aromatic heterocycle, each of which may be substituted.

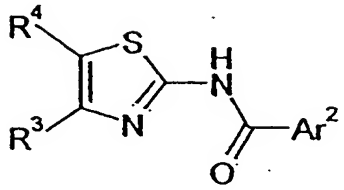
(7) The compound according to (6), wherein R^3 is phenyl or thienyl, each or which may be substituted; R^4 is a group represented by the general Formula (II); Ar^2 is phenyl or pyridyl, each of which may be substituted.

(8) The compound according to (7), wherein n is 2, m is 2, and X is a group represented by N-R^{26} or C(-R^{27})-R^{28}.

(9) The compound according to (8), wherein R^3 is phenyl or thienyl, each of which is substituted with 1 to 3 halogen atoms (when substituted with 2 or 3 halogen atoms, the halogen atoms may be identical or different.).

(10) The compound according to (9), wherein R^4 is 4-(piperidin-1-yl)piperidin-1-yl, 4-propylpiperidin-1-yl, 4-cyclohexylpiperazin-1-yl, or 4-propylpiperazin-1-yl.

Appendix A5



(V)

wherein symbols have the following meaning,

Ar^2: a group represented by Ar^1 as described in (1), with the proviso that indol-2-yl is excluded,

R^3: a group represented by R^1 as described in (1),

R^4: a group represented by R^2 as described in (1), with the proviso that a group represented by the general Formula (IV) is excluded.

Ar^2 in the compound of the general Formula (V) is preferably phenyl or monocyclic aromatic heterocycle, each of which may be substituted;

more preferably, phenyl or pyridyl, each of which may be substituted;

still more preferably, phenyl which is unsubstituted at 2- and 6-positions, substituted with -H, -F, -Cl, or -Br at 3-position, substituted with -F, -Cl, or -Br at 5-position, and substituted at 4-position, or pyridin-3-yl which is unsubstituted at 2- and 4-positions, substituted with -F, -Cl, or -Br at 5-position, and substituted at 6- position;

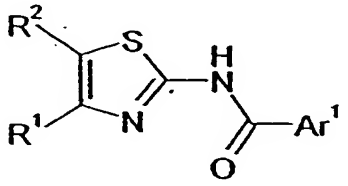
most preferably, phenyl substituted at 4-position with a substituent group selected from the group consisting of $-O-R^Y$, $-NH-R^Y$, optionally substituted piperidin-1-yl and optionally substituted piperazin-1-yl, or pyridin-3-yl which is substituted at 6-position with a substituent group selected from the group consisting of $-O-R^Y$, $-NH-R^Y$, optionally substituted piperidin-1-yl and optionally substituted piperazin-1-yl.

R^3 in the compound of the general Formula (V) is preferably phenyl or

Appendix A5
cont'd

The present invention relates to the following aspects (1)~(17).

(1) A pharmaceutical composition for increasing the number of platelets comprising a 2-acylaminothiazole derivative represented by the following general Formula (I) or a pharmaceutically acceptable salt thereof as an active ingredient:



(I)

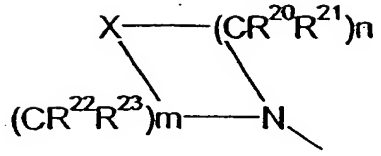
wherein symbols have the following meanings:

Ar^1: aryl, monocyclic aromatic heterocycle, or bicyclic condensed heterocycle, each of which may be substituted (with the proviso that when R^1 is aryl or pyridyl, each of which may be substituted with one or more groups selected from the group consisting of lower alkyl, -CO-lower alkyl, -COO-lower alkyl, -OH, -O-lower alkyl, -OCO-lower alkyl, and halogen atom, and R^2 is a group represented by the following general Formula (II); Ar^1 is not phenyl or pyridyl, each of which may be substituted with one or more groups selected from the group consisting of lower alkyl, -CO-lower alkyl, -COO-lower alkyl, -OH, -O-lower alkyl, -OCO-lower alkyl, and halogen atom.),

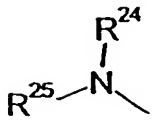
R^1: aryl or monocyclic aromatic heterocycle, each of which may be substituted,

R^2: a group represented by the following general Formula (II), (III) or (IV):

Appendix A5
cont'd



(II)



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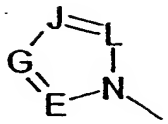


(IV)

wherein symbols have the following meanings:

n: an integer of 1 to 3,

m: an integer of 1 to 3,

(when n or m is an integer of 2 or more, $CR^{20}R^{21}$ and $CR^{22}R^{23}$ may be identical or different.)

X: O, S, or a group represented by N-R^{26} or C(-R^{27})-R^{28},

E, G, J, L: independently N or a group represented by C-R^{29}, with the proviso that at least one of them is C-R^{29},

R^{20}, R^{21}, R^{22}, R^{23}, R^{26}, R^{27}, R^{28}, R^{29}: which may be identical or different -H; -OH; -O-lower alkyl; optionally substituted lower alkyl; optionally substituted cycloalkyl; optionally substituted aryl; optionally substituted arylalkyl; optionally substituted aromatic heterocycle; optionally substituted aromatic heterocyclic alkyl; optionally substituted nonaromatic heterocycle; optionally substituted lower alkenyl; optionally substituted lower alkylidene; -COOH; -COO-lower alkyl; -COO-lower alkenyl; -COO-lower alkylene-aryl; -COO-lower alkylene-aromatic heterocycle; carbamoyl or amino, each of which may be substituted with one or more groups selected from the group consisting of lower alkyl and cycloalkyl, each of which may be substituted with halogen, -OH, -O-lower alkyl, or -O-aryl; -NHCO-lower alkyl; or oxo.

R^{24}, R^{25}: which may be identical or different, -H, optionally substituted lower alkyl, optionally substituted cycloalkyl, or optionally substituted

Appendix A5
cont'd

thienyl, each of which may be substituted; more preferably, phenyl or thienyl, each of which may be substituted with one or more groups selected from the group consisting of halogen atom and trifluoromethyl; still more preferably, phenyl or thienyl, each of which is substituted with 1 to 3 halogen atoms (when substituted with 2 or 3 halogen atoms, the halogen atom may be identical or different.)

R^4 in the compound of the general Formula (V) is preferably a group represented by the general Formula (II), more preferably a group represented by the general Formula (II) wherein n is 2, m is 2, and X is N-R^{26} or C-(R^{27})-R^{28}; still more preferably, 4-(piperidin-1-yl)piperidin-1-yl, 4-propylpiperidin-1-yl, 4-cyclohexylpiperazin-1-yl, or 4-propylpiperazin-1-yl.

(6) The compound according to (5), wherein Ar^2 is phenyl or monocyclic aromatic heterocycle, each of which may be substituted.

(7) The compound according to (6), wherein R^3 is phenyl or thienyl, each or which may be substituted; R^4 is a group represented by the general Formula (II); Ar^2 is phenyl or pyridyl, each of which may be substituted.

(8) The compound according to (7), wherein n is 2, m is 2, and X is a group represented by N-R^{26} or C(-R^{27})-R^{28}.

(9) The compound according to (8), wherein R^3 is phenyl or thienyl, each of which is substituted with 1 to 3 halogen atoms (when substituted with 2 or 3 halogen atoms, the halogen atoms may be identical or different.).

(10) The compound according to (9), wherein R^4 is 4-(piperidin-1-yl)piperidin-1-yl, 4-propylpiperidin-1-yl, 4-cyclohexylpiperazin-1-yl, or 4-propylpiperazin-1-yl.

Appendix B

Table I

Application No.	Page/line	Substituent	Scope
JP Priority App. No. 2002-10413	Page 9, lines 1-11	R^3-R^6	which may be identical or different, –H; -OH; -O-lower alkyl; optionally substituted lower alkyl; optionally substituted cycloalkyl; optionally substituted aryl; optionally substituted aralkyl; optionally substituted aromatic heterocycle; optionally substituted heteroarylalkyl; optionally substituted nonaromatic heterocycle; lower alkenyl; lower alkylidene; -COOH; -COO-lower alkyl; -COO-lower alkenyl; -COO-lower alkylene-aryl; -COO-lower alkylene-aromatic heterocycle; carbamoyl or amino, each of which may be substituted with one or more groups selected from the group consisting of lower alkyl which may be substituted with halogen, -OH, -O-lower alkyl, or -O-aryl, and cycloalkyl; -NHCO-lower alkyl; and oxo.
JP Priority App. No. 2002-10447	Page 8, line 13, to page 9, line3	R^3-R^6	which may be identical or different, –H; -OH; -O-lower alkyl; optionally substituted lower alkyl; optionally substituted cycloalkyl; optionally substituted aryl; optionally substituted aralkyl; optionally substituted aromatic heterocycle; optionally substituted heteroarylalkyl; optionally substituted nonaromatic heterocycle; lower alkenyl; lower alkylidene; -COOH; -COO-lower alkyl; -COO-lower alkenyl; -COO-lower alkylene-aryl; -COO-lower alkylene-aromatic heterocycle; carbamoyl or amino, each of which may be substituted with one or more groups selected from the group consisting of lower alkyl which may be substituted with halogen, -OH, -O-lower alkyl, or -O-aryl, and cycloalkyl; -NHCO-lower alkyl; and oxo.
U.S. 10/500,964	Amended claims 5 and 37	R^{20}-R^{23}	is independently selected from the group consisting of –H; -OH; -O-lower alkyl; optionally substituted lower alkyl; optionally substituted cycloalkyl; optionally substituted aryl; optionally substituted arylalkyl; optionally substituted aromatic heterocycle; optionally substituted aromatic heterocyclic-alkyl; optionally substituted nonaromatic heterocycle; lower alkenyl; lower alkylidene; -COOH; -COO-lower alkyl; -COO-lower alkenyl; -COO-lower alkylene-aryl; -COO-lower alkylene-aromatic heterocycle; carbamoyl or amino, each of which may be substituted with one or more groups selected from the group consisting of lower alkyl which may be substituted with halogen, -OH, -O-lower alkyl, or -O-aryl, and cycloalkyl; -NHCO-lower alkyl; and oxo.

Appendix C

Table II

Application No.	Page/line	Substituent	Scope
JP Priority App. No. 2002-10413	Page 9, lines 1-11	R^9-R^{11}	which may be identical or different, –H; -OH; -O-lower alkyl; optionally substituted lower alkyl; optionally substituted cycloalkyl; optionally substituted aryl; optionally substituted aralkyl; optionally substituted aromatic heterocycle; optionally substituted heteroaralkyl; optionally substituted nonaromatic heterocycle; lower alkenyl; lower alkylidene; -COOH; -COO-lower alkyl; -COO-lower alkenyl; -COO-lower alkylene-aryl; -COO-lower alkylene-aromatic heterocycle; carbamoyl or amino, each of which may be substituted with one or more groups selected from the group consisting of lower alkyl which may be substituted with halogen, -OH, -O-lower alkyl, or -O-aryl, and cycloalkyl; -NHCO-lower alkyl; and oxo.
JP Priority App. No. 2002-10447	Page 8, line 13, to page 9, line3	R^9-R^{11}	which may be identical or different, –H; -OH; -O-lower alkyl; optionally substituted lower alkyl; optionally substituted cycloalkyl; optionally substituted aryl; optionally substituted aralkyl; optionally substituted aromatic heterocycle; optionally substituted heteroaralkyl; optionally substituted nonaromatic heterocycle; lower alkenyl; lower alkylidene; -COOH; -COO-lower alkyl; -COO-lower alkenyl; -COO-lower alkylene-aryl; -COO-lower alkylene-aromatic heterocycle; carbamoyl or amino, each of which may be substituted with one or more groups selected from the group consisting of lower alkyl which may be substituted with halogen, -OH, -O-lower alkyl, or -O-aryl, and cycloalkyl; -NHCO-lower alkyl; and oxo.
U.S. 10/500,964	Amended claims 5 and 37	R^{26}-R^{28}	is independently selected from the group consisting of –H; -OH; -O-lower alkyl; optionally substituted lower alkyl; optionally substituted cycloalkyl; optionally substituted aryl; optionally substituted aralkyl; optionally substituted aromatic heterocycle; optionally substituted aromatic heterocycle-alkyl; optionally substituted nonaromatic heterocycle; lower alkenyl; lower alkylidene; -COOH; -COO-lower alkyl; -COO-lower alkenyl; -COO-lower alkylene-aryl; -COO-lower alkylene-aromatic heterocycle; carbamoyl or amino, each of which may be substituted with one or more groups selected from the group consisting of lower alkyl which may be substituted with halogen, -OH, -O-lower alkyl, or -O-aryl, and cycloalkyl; -NHCO-lower alkyl; and oxo.

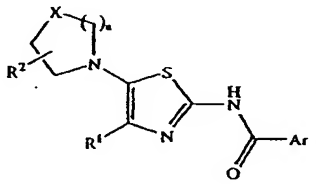
Appendix D

platelet increasing activity. As a result, it has been found that a novel 2-acylaminothiazole derivative has a superior platelet increasing activity, leading to accomplishment of the invention.

[0015] The compound of the invention is a 2-acylaminothiazole derivative structurally characterized in that an acylamino group is substituted at the 2-position thereof and that a nitrogen atom of a nitrogen-containing heterocycle is directly bound to the 5-position thereof. Further, the compound of the invention is pharmacologically characterized by having a platelet increasing activity based on a megakaryocyte colony formation promoting action.

[0016] Specifically, according to the invention, there is provided a 2-acylaminothiazole derivative represented by the following general formula (I) or a pharmaceutically acceptable salt thereof, which is useful as a therapeutic agent for thrombocytopenia.

(I)



[0017] In the formula, the symbols have the following meanings:

[0018] Ar represents phenyl or pyridyl, each of which may be substituted with one or more groups selected from the group consisting of lower alkyl, —CO-lower alkyl, —COO-lower alkyl, —OH, —O-lower alkyl, —OCO-lower alkyl, and halogen;

[0019] R^1 represents aryl or pyridyl, each of which may be substituted with one or more groups selected from the group consisting of lower alkyl, —CO-lower alkyl, —COO-lower alkyl, —OH, —O-lower alkyl, —OCO-lower alkyl, and halogen;

[0020] R^2 represents a group selected from the group consisting of —H, —OH, —COOH, —COO-lower alkyl, carbamoyl which may be substituted with one or two lower alkyls, amino which may be substituted with one or two lower alkyls, and cyclic amino, provided that one or more of this group may be present on the ring;

[0021] —X— represents $—CH_2—$, —O—, —S—, or $—N(R^3)—$;

[0022] R^3 represents optionally substituted lower alkyl, cycloalkyl, optionally substituted aryl, optionally substituted aryl-lower alkyl, optionally substituted heteroaryl, optionally substituted heteroaryl-lower alkyl, —CO-lower alkyl, —COO-lower alkyl, or carbamoyl which may be substituted one or two lower alkyls; and

[0023] n represents an integer of from 1 to 3.

[0024] Compounds represented by the foregoing general formula (I), wherein X represents $—N(R^3)—$, and n is 2 or 3, or pharmaceutically acceptable salts thereof are preferable. Compounds represented by the foregoing general formula (I), wherein X represents $—N(R^3)—$, n is 2 or 3, and Ar represents phenyl or pyridyl, each of which may be substituted with one or more groups selected from the group consisting of —OH, —O-lower alkyl, and —OCO-lower alkyl, or pharmaceutically acceptable salts thereof are more preferable. Particularly preferred examples include:

[0025] 3,5-dimethoxy-N-(5-morpholin-4-yl-4-phenylthiazol-2-yl)benzamide, N-[5-(4-cyclohexylpiperazin-1-yl)-4-(4-fluorophenyl)thiazol-2-yl]-2-methoxyisonicotinamide,

[0026] 3-chloro-N-[5-(4-cyclohexylpiperazin-1-yl)-4-(4-fluorophenyl)thiazol-2-yl]-4-hydroxybenzamide,

[0027] 3,5-dimethoxy-N-(5-piperidin-1-yl-4-pyridin-4-ylthiazol-2-yl)benzamide, or

[0028] 4-{[5-(4-cyclohexylpiperazin-1-yl)-4-phenylthiazol-2-yl]carbamoyl}phenyl acetate, or

[0029] pharmaceutically acceptable salts thereof.

[0030] Further, according to the invention, there is provided a pharmaceutical composition comprising, as an active ingredient, a compound represented by the foregoing general formula (I); a compound represented by the foregoing general formula (I), wherein X represents $—N(R^3)—$, and n is 2 or 3; a compound represented by the foregoing general formula (I), wherein X represents $—N(R^3)—$, n is 2 or 3, and Ar represents phenyl or pyridyl, each of which may be substituted with one or more groups selected from the group consisting of —OH, —O-lower alkyl, and —OCO-lower alkyl; or a pharmaceutically acceptable salt thereof. Concretely, the foregoing pharmaceutical composition is a pharmaceutical composition as a megakaryocyte colony forming promoter, a pharmaceutical composition as a platelet increasing agent, or a pharmaceutical composition as a therapeutic agent for thrombocytopenia.

[0031] The compounds of the invention will be further described below.

[0032] In this description, the term "lower alkyl" means a linear or branched carbon chain having from 1 to 6 carbon atoms (C_{1-6}), and specific examples include methyl, ethyl, propyl, isopropyl, butyl, tert-butyl, pentyl, neopentyl, and hexyl, etc. Of these are preferable C_{1-3} alkyls including methyl, ethyl, propyl and isopropyl. Examples of the substituent acceptable in the "optionally substituted lower alkyl" for R^3 include —O-lower alkyl and —O-aryl, etc.

[0033] The term "aryl" means an aromatic ring comprising carbon atoms and is preferably a monocyclic to tricyclic aromatic ring having from 6 to 14 carbon atoms (C_{6-14}). Specific examples include phenyl and naphthyl, with phenyl being preferred. Examples of the substituent acceptable in the "optionally substituted aryl" and "optionally substituted aryl-lower alkyl" for R^3 include lower alkyl, —O-lower alkyl, halogen, nitro, and cyano, etc.

[0034] The term "heteroaryl" means a monovalent group of a monocyclic to tricyclic aromatic ring having one or more hetero atom such as nitrogen, oxygen, and sulfur, and specific examples include pyridyl, pyrazyl, pyridazyl, pyrrolyl, imidazolyl, thienyl, furanyl, thiazolyl, oxazolyl, indolyl, quinolyl, and benzothiazolyl, etc. Examples of the